

Rusty Worms in the Brain

February 25 2008

Iron is vital to human life; for example, it is a component of hemoglobin, the substance that makes our blood red and supplies our cells with oxygen. However, iron can also cause heavy damage; it is thought that iron deposits in the brain contribute to certain forms of neurodegenerative diseases such as Parkinson's, Huntington's, and Alzheimer's.

A malfunction of the blood transporter transferrin may be to blame. A team led by Peter J. Sadler at the University of Warwick (Coventry, UK) and Sandeep Verma of the Indian Institute of Technology (Kanpur, India) has now been able to show that transferrin can clump together to form wormlike fibrils. As reported in the journal *Angewandte Chemie*, this process releases rustlike iron particles.

Within the body, iron is present in the form of iron ions with a threefold positive charge (Fe^{3+}) and must always be well “wrapped” to prevent it from reacting with proteins and causing damage. In blood plasma, iron is carried in the “pockets” of the iron transport protein transferrin. It only gets unwrapped once it is inside special cellular organelles.

But things can go wrong in this system, as Sadler and his colleagues have now proven. The researchers deposited iron-loaded human transferrin onto various surfaces under conditions that emulate those in living organisms. By using microscopy and electron microscopy, the researchers showed that the proteins aggregate into long wormlike fibrils. These “worms” have a regular striped pattern; the narrow dark stripes contain something similar to rust. “Within the fibrils, the iron

ions are no longer properly enclosed;” explains Sadler, “instead, they aggregate into periodically arranged nanocrystals whose structure seems to be very similar to the iron oxide mineral lepidocrocite”.

The researchers suspect that in certain forms of neurodegenerative disease, iron deposits may form in a similar fashion in the brain. Such iron crystals are highly reactive and could lead to the formation of toxic free radicals, which attack and destroy nerve cells. If this assumption can be verified in vivo, agents that hinder the aggregation of transferrin may be the foundation for a new family of drugs.

Citation: Peter J. Sadler, Periodic Iron Nanomineralization in Human Serum Transferrin Fibrils, *Angewandte Chemie International Edition* 2008, 47, No. 12, 2221–2231, doi: 10.1002/anie.200705723

Source: Angewandte Chemie

Citation: Rusty Worms in the Brain (2008, February 25) retrieved 26 April 2024 from <https://phys.org/news/2008-02-rusty-worms-brain.html>

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